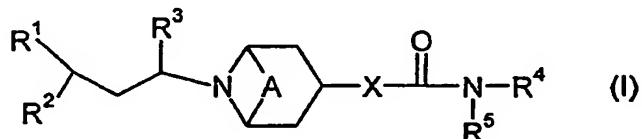


CLAIMS

1. A compound of formula (I):



5 wherein

A is absent or is $(CH_2)_2$;

R¹ is C₁₋₈ alkyl, C(O)NR¹⁰R¹¹, C(O)₂R¹², NR¹³C(O)R¹⁴, NR¹⁵C(O)NR¹⁶R¹⁷,

NR¹⁸C(O)₂R¹⁹, heterocyclyl, aryl or heteroaryl;

R¹⁰, R¹³, R¹⁵, R¹⁶ and R¹⁸ are hydrogen or C₁₋₆ alkyl;

10 R¹¹, R¹², R¹⁴, R¹⁷ and R¹⁹ are C₁₋₈ alkyl (optionally substituted by halo, hydroxy, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₆ cycloalkyl (optionally substituted by halo), C₅₋₆ cycloalkenyl, S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O)₂(C₁₋₄ alkyl), heteroaryl, aryl, heteroaryloxy or aryloxy), aryl, heteroaryl, C₃₋₇ cycloalkyl (optionally substituted by halo or C₁₋₄ alkyl), C₄₋₇ cycloalkyl fused to a phenyl ring, C₅₋₇ cycloalkenyl, or, heterocyclyl (itself optionally substituted by oxo, C(O)(C₁₋₆ alkyl), S(O)_k(C₁₋₆ alkyl), halo or C₁₋₄ alkyl); or R¹¹, R¹², R¹⁴ and R¹⁷ can also be hydrogen;

15 or R¹⁰ and R¹¹, and/or R¹⁶ and R¹⁷ may join to form a 4-, 5- or 6-membered ring which optionally includes a nitrogen, oxygen or sulphur atom, said ring being optionally substituted by C₁₋₆ alkyl, S(O)_l(C₁₋₆ alkyl) or C(O)(C₁₋₆ alkyl);

20 R² C₁₋₆ alkyl, phenyl, heteroaryl or C₃₋₇ cycloalkyl;

R³ H or C₁₋₄ alkyl;

R⁴ is aryl or heteroaryl;

R⁵ is H or alkyl;

X is CH₂, (CH₂)₂, CH=CH, OCH₂ or S(O)_nCH₂;

25 n is 0, 1 or 2;

unless specified otherwise aryl, phenyl and heteroaryl moieties are independently optionally substituted by one or more of halo, cyano, nitro, hydroxy, OC(O)NR²⁰R²¹, NR²²R²³, NR²⁴C(O)R²⁵, NR²⁶C(O)NR²⁷R²⁸, S(O)₂NR²⁹R³⁰, NR³¹S(O)₂R³²,

C(O)NR³³R³⁴, CO₂R³⁶, NR³⁷CO₂R³⁸, S(O)_qR³⁹, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl,

30 C₃₋₁₀ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy(C₁₋₆ alkyl), C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, phenyl, phenyl(C₁₋₄ alkyl), phenoxy, phenylthio, phenylS(O), phenylS(O)₂, phenyl(C₁₋

4) alkoxy, heteroaryl, heteroaryl(C₁₋₄)alkyl, heteroaryloxy or heteroaryl(C₁₋₄)alkoxy; wherein any of the immediately foregoing phenyl and heteroaryl moieties are optionally substituted with halo, hydroxy, nitro, S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O)₂(C₁₋₄ alkyl), S(O)₂NH₂, S(O)₂NH(C₁₋₄ alkyl), S(O)₂N(C₁₋₄ alkyl)₂, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, C(O)NH₂, C(O)NH(C₁₋₄ alkyl), C(O)N(C₁₋₄ alkyl)₂, CO₂H, CO₂(C₁₋₄ alkyl), NHC(O)(C₁₋₄ alkyl), NHS(O)₂(C₁₋₄ alkyl), CF₃ or OCF₃;

5 unless otherwise stated heterocyclyl is optionally substituted by C₁₋₆ alkyl [optionally substituted by phenyl {which itself optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, OCF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)} or heteroaryl {which itself optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, OCF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}], phenyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, OCF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}, heteroaryl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}, S(O)₂NR⁴⁰R⁴¹, C(O)R⁴², C(O)₂(C₁₋₆ alkyl) (such as tert-butoxycarbonyl), C(O)₂(phenyl(C₁₋₂ alkyl)) (such as benzyloxycarbonyl), C(O)NHR⁴³, S(O)₂R⁴⁴, NHS(O)₂NHR⁴⁵, NHC(O)R⁴⁶, NHC(O)NHR⁴⁷ or NHS(O)₂R⁴⁸, provided none of these last four substituents is linked to a ring nitrogen;

10 k, l, p and q are, independently, 0, 1 or 2;

15 R²⁰, R²², R²⁴, R²⁶, R²⁷, R²⁹, R³¹, R³³, R³⁷ and R⁴⁰ are, independently, hydrogen or C₁₋₆ alkyl;

20 R²¹, R²³, R²⁵, R²⁸, R³⁰, R³², R³⁴, R³⁶, R³⁸, R³⁹, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, R⁴⁷ and R⁴⁸ are, independently, C₁₋₆ alkyl (optionally substituted by halo, hydroxy, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₆ cycloalkyl, C₅₋₆ cycloalkenyl, S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O)₂(C₁₋₄ alkyl), heteroaryl, phenyl, heteroaryloxy or phenoxy), C₃₋₇ cycloalkyl, phenyl or heteroaryl; wherein any of the immediately foregoing phenyl and heteroaryl moieties are optionally substituted with halo, hydroxy, nitro, S(C₁₋₄ alkyl), S(O)(C₁₋₄ alkyl), S(O)₂(C₁₋₄ alkyl), S(O)₂NH₂, S(O)₂NH(C₁₋₄ alkyl), S(O)₂N(C₁₋₄ alkyl)₂, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, C(O)NH₂, C(O)NH(C₁₋₄ alkyl), C(O)N(C₁₋₄ alkyl)₂, CO₂H, CO₂(C₁₋₄ alkyl), NHC(O)(C₁₋₄ alkyl), NHS(O)₂(C₁₋₄ alkyl), C(O)(C₁₋₄ alkyl), CF₃ or OCF₃;

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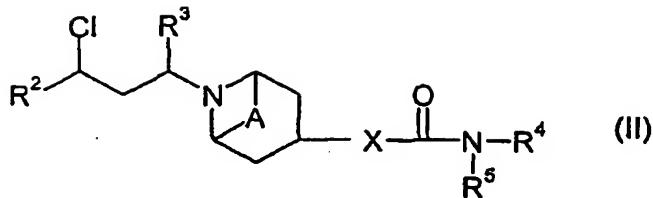
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R^{21} , R^{23} , R^{25} , R^{28} , R^{30} , R^{34} , R^{35} , R^{36} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} and R^{47} may additionally be hydrogen;

or a pharmaceutically acceptable salt thereof or a solvate thereof.

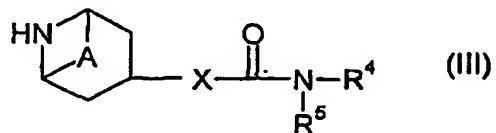
- 5 2. A compound as claimed in claim 1 wherein A is absent.
3. A compound as claimed in claim 1 or 2 wherein R^1 is piperidinyl or piperazinyl substituted by $S(O)_2C_{1-4}$ alkyl, $S(O)_2C_{1-4}$ haloalkyl or $C(O)NH$ -phenyl.
- 10 4. A compound as claimed in claim 1 or 2 wherein R^1 is phenyl substituted by $S(O)_2C_{1-4}$ alkyl.
5. A compound as claimed in claim 1, 2 or 3 wherein R^2 is phenyl optionally substituted by 0, 1 or 2 fluorines.
- 15 6. A compound as claimed in claim 1, 2, 3, 4 or 5 wherein R^3 is hydrogen.
7. A compound as claimed in any one of the preceding claims wherein R^4 is phenyl or benzyl, either of which is optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_2(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein z is 0, 1 or 2.
- 20 8. A compound as claimed in any one of the preceding claims wherein R^5 is hydrogen.
9. A compound as claimed in any one of the preceding claims wherein X is CH_2 or $CH=CH$.
- 25 10. A compound of formula (I) as claimed in claim 1 can be prepared by:
 - a. for a compound of the invention wherein R^1 is an N-linked optionally substituted heterocycle, reacting a compound of formula (II):

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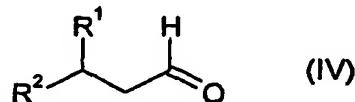


wherein R^2 , R^3 , R^4 , R^5 , A and X are as defined in claim 1, with a compound R^1H (wherein the H is on a heterocycle ring nitrogen atom) wherein R^1 is as defined in claim 1, in the presence of a suitable base, in a suitable solvent;

5 b. for a compound of the invention wherein R^3 is hydrogen, coupling a compound of formula (III):

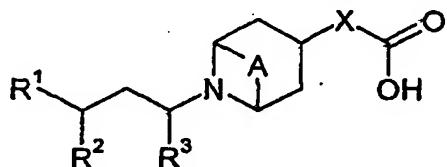


wherein R^4 , R^5 , A and X are as defined in claim 1, with a compound of formula (IV):



10 wherein R^1 and R^2 are as defined in claim 1, in the presence of $NaBH(OAc)_3$ (wherein Ac is $C(O)CH_3$) in a suitable solvent at room temperature;

c. activating the acid group of a compound of formula (V)



15 wherein X, A, R^1 , R^2 and R^3 are as defined in claim 1, and coupling the product so formed with an amine R^4R^5NH (wherein R^4 and R^5 are as defined in claim 1).

20 11. A pharmaceutical composition which comprises a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, and a pharmaceutically acceptable adjuvant, diluent or carrier.

12. A compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, for use as a medicament.
13. A compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, in the manufacture of a medicament for use in therapy.
14. A method of treating a CCR5 mediated disease state comprising administering to a patient in need of such treatment an effective amount of a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof.